REMARKS

The Present Invention

The present invention pertains to a method of inhibiting binding of a chaperone protein with its client protein or client polypeptide by contacting a chaperone protein with a coumarin or a coumarin derivative.

The Pending Claims

Claims 1-17 and 22 are currently pending. Claims 18-21 and 23 have been canceled as being drawn to a non-elected invention. Claims 1-17 and 22 are directed to a method of inhibiting a chaperone protein with its client protein or client polypeptide by contacting a chaperone protein with a coumarin or a coumarin derivative.

Summary of the Office Action

Claims 1, 3-6, 9-15, and 22 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled. Claims 1, 2, 8-15 and 22 have been rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Casley-Smith et al. (U.S. Patent No. 5,096,887) (hereinafter "Casley-Smith et al."). Claims 1-7, 16, 17, and 22 have been rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Civitico et al. *J. Med. Virology*, 31: 90-97 (1990) (hereinafter "Civitico et al.") Claims 1-3, 5-15, and 22 have been rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Kennedy et al. *J. Clin. Oncology*, 13(5):1136-1143 (1995) (hereinafter "Kennedy et al."). Claims 1, 3, 5-10, 12-14 and 22 have been rejected under 35 U.S.C. § 102(e), as allegedly anticipated by Styczynski et al. (U.S. Patent No. 6,037,326) (hereinafter "Styczynski et al."). Reconsideration of the pending claims is respectfully requested.

Discussion of the Section 112, First Paragraph, Rejection

Claims 1, 3-6, 8-15, and 22 have been rejected as allegedly not enabled for a method of inhibiting the binding of a chaperone protein with its client protein by contacting a chaperone protein other than Hsp90 with a coumarin or a coumarin derivative. The rejection is respectfully traversed for the reasons set forth below.

The Office specifically alleges that the specification only teaches the claimed method wherein the chaperone protein is Hsp90, and thus, the specification does not enable one of ordinary skill in the art to make and/or use the present invention to inhibit the binding of any other chaperone protein with its client protein/polypeptide. As acknowledged in the most recent Office Action (page 3), the instant application, as well as Jolley et al., *J. Nat'l Cancer Inst.*, 92:1564-1572 (2000) (hereinafter "Jolley et al."), disclose a variety of different proteins

that act as molecular chaperones. Further, the assays conducted in the instant application, Examples 1-4 at, for example, page 13, line 27, through page 16, line 24, teach those of ordinary skill how to make and use the claimed invention to the full scope of the claims. Specifically, Example 1, at page 13, line 27, through page 14, line 17, demonstrates the binding of a chaperone protein to a coumarin or a coumarin derivative. Likewise, Example 3, at page 15, lines 21-36, demonstrates a decrease in the level of client protein/polypeptide post contact between a chaperone protein and a coumarin or a coumarin derivative. Such disclosure provides a sufficient teaching for one of ordinary skill in the art to identify other chaperone proteins that are inhibited in client protein interactions post contact with a coumarin or coumarin derivative. The fact that the assays are conducted using Hsp90 does not limit the scope of the claims to such a protein.

Thus, enablement is provided by the specification in the form of a list of candidate chaperone proteins as well as specific assays to identify chaperone proteins useful in the method defined by the pending claims. A person of ordinary skill in the art would know how to conduct the assays with each candidate chaperone protein. Indeed, such assays constitute no more than routine screening for the skilled artisan. As stated by the Federal Circuit, "[e]nablement is not precluded by the necessity for some experimentation such as routine screening." *In re Wands*, 858 F.2d 731, 736-737 (Fed. Cir. 1988).

In view of the foregoing, Applicants submit that the specification is enabling for one ordinarily skilled in the art to make and use the present invention. Therefore, Applicants hereby request that the rejection of claims 1, 3-6, 8-15, and 22 for alleged lack of enablement be withdrawn.

Discussion of Rejections under U.S.C. § 102

A single prior art reference must disclose each and every limitation of a claimed invention, either explicitly or inherently, to anticipate the claimed invention. *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999). None of the references relied on by the Office to support the anticipation rejections explicitly disclosure all the limitations of the rejected claims. Further, all the Section 102 rejections made by the Office rely on the view that the cited references *inherently* disclose one or more elements of the rejected claims. While the disclosure of a claim limitation can be inherent, rather than explicit, in a reference, the disclosure of limitations in a reference may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient to establish the inherent disclosure of that thing. Inherency must be established as a necessary consequence of what was intended. *Id.* at 1366. As succintly stated in the M.P.E.P., "[i]n relying upon the theory of inherency, the [E]xaminer must

provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art." M.P.E.P. § 2112 (emphasis added). The inherency aspect of each of the anticipation rejections is discussed below, followed by the reasons why the anticipation rejections are improper.

Claims 1, 2, 8-15 and 22 are allegedly anticipated by Casley-Smith et al. Since Casley-Smith et al. reportedly discloses administering benzo-pyrone for treating edemas, the Office concludes that the administered benzo-pyrone also necessarily binds endogenous chaperone protein Hsp90, in addition to treating edema.

Claims 1-7, 16, 17 and 22 are allegedly anticipated by Civitico et al. The Office alleges that, since Civitico et al. discloses administering antiviral compounds to primary duck hepatocytes infected with duck hepatitis B virus, of which, two of the compounds fall in the class of a coumarin or a coumarin derivative, the administered compounds also necessarily bind the allegedly endogenous chaperone protein Hsp90, in addition to treating duck hepatitis B virus.

Claims 1-3, 5-15, and 22 are allegedly anticipated by Kennedy et al. The Office alleges that, since Kennedy et al. discloses the combinatorial use of novobiocin with clophosphamide and thiotepa for treating breast cancer, the administered novobiocin also necessarily binds endogenous chaperone protein Hsp90, in addition to being used in combinatorial therapy for breast cancer.

Finally, claims 1, 3, 5-10, 12-14, and 22 are allegedly anticipated by Styczynski et al. The Office alleges that, since Styczynski et al. discloses a topical administration of topoisomerase inhibitors to reduce unwanted mammalian hair growth, a coumarin topically administered as a topoisomerase inhibitor also necessarily binds topically expressed chaperone protein Hsp90, in addition to reducing unwanted hair growth.

Anticipation by inherency requires the Office to provide a basis in fact to reasonably support that the allegedly inherent characteristics *necessarily* flow from the teachings of the prior art. Here, the Office has failed to satisfy its burden for proving inherency. For each anticipation rejection, the Office relies on the belief that Hsp90 is constitutively expressed in cells in a manner that the compounds described in the cited references necessarily contact Hsp90 when the compounds are administered as described in those references. However, the Office provides no evidence that a coumarin or coumarin derivative will necessarily contact endogenous Hsp90 protein and inhibit chaperone protein-client protein/polypeptide interactions if administered according to the cited references such that the pending claims are anticipated. Although there may be a possibility that such a contact may occur between a coumarin or a coumarin derivative and an Hsp90 protein, wherein the Hsp90 protein is then

inhibited to interact with its client protein/polypeptide, such a result does not necessarily flow from the teachings of the prior art, especially in the absence of further technical information such as the location of expression, the level of expression, and the affinity between a coumarin or a coumarin derivative and Hsp90. Therefore, the Office has not satisfied its burden to establish anticipation by inherency for any of the references cited as anticipatory.

For example, in Civitico et al., primary duck hepatocytes are the model system whereby the Office alleges that administered coumarins or coumarin derivatives inherently associate with endogenous Hsp90. The Office has not provided evidence of the presence of heat shock protein, let alone Hsp90, in duck hepatocytes. Moreover, even if Hsp90 is present in duck hepatocytes, which Applicants neither affirm nor deny, no reasonable support is set forth by the Office to provide a basis for the proposition that any chaperone protein is necessarily being contacted by a coumarin or a coumarin derivative and, as a result, necessarily inhibited from interacting with its client protein/polypeptide.

Similarly, Kennedy et al. discloses a combinatorial treatment wherein a coumarin is one of three compounds administered to patients with breast cancer. Again, the Office has not provided any support for its rejection based on inherent anticipation other than the statement that one of the three administered compounds necessarily binds Hsp90. In this instance, even if the administered coumarin does contact Hsp90 protein when administered to a patient, the contact may not necessarily inhibit the interaction of Hsp90 with its client protein/polypeptide.

Casley-Smith et al. and Styczynski et al. are similarly deficient, with the Office not providing any evidence that demonstrates that these references inherently disclose the binding of endogenous Hsp90 protein with a coumarin or a coumarin derivative so as to necessarily inhibit the interaction of Hsp90 with its client protein/polypeptide.

In view of the foregoing, Applicants respectfully submit that the Office has not satisfied its burden to demonstrate that any of the cited references anticipate the subject matter of any of the pending claims. Therefore, Applicants submit that the rejections under Section 102 are improper and request that the rejections be withdrawn.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

John Kulyk, Jr., Reg. No. 30,763
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

Date: May 10, 2004